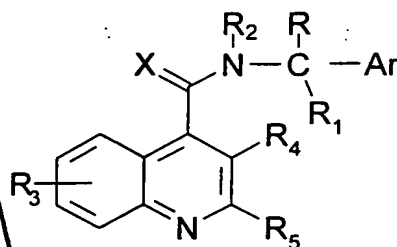


Claims

1. A compound, or solvate or salt thereof, of formula (I):



(I)

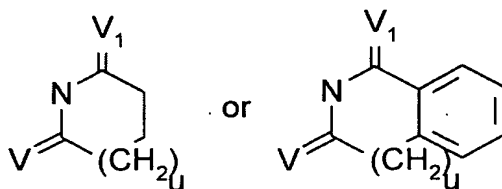
in which:

Ar is an optionally substituted phenyl, naphthyl or C₅₋₇ cycloalkdienyl group, or an optionally substituted single or fused ring heterocyclic group, having aromatic character, containing from 5 to 12 ring atoms and comprising up to four hetero-atoms in the or each ring selected from S, O, N;

R is linear or branched C₁₋₈ alkyl, C₃₋₇ cycloalkyl, C₄₋₇ cycloalkylalkyl, optionally substituted phenyl or phenyl C₁₋₆ alkyl, an optionally substituted five-membered heteroaromatic ring comprising up to four heteroatoms selected from O and N, hydroxy C₁₋₆ alkyl, amino C₁₋₆ alkyl, C₁₋₆ alkylaminoalkyl, di-C₁₋₆ alkylaminoalkyl, C₁₋₆ acylaminoalkyl, C₁₋₆ alkoxyalkyl, C₁₋₆ alkylcarbonyl, carboxy, C₁₋₆ alkoxyxcarbonyl, C₁₋₆ alkoxyxcarbonyl, C₁₋₆ alkyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, di C₁₋₆ alkylaminocarbonyl, halogeno C₁₋₆ alkyl; or is a group -(CH₂)_p- when cyclized onto Ar, where p is 2 or 3.

R₁ and R₂, which may be the same or different, are independently hydrogen or C₁₋₆ linear or branched alkyl, or together form a -(CH₂)_n- group in which n represents 3, 4, or 5; or R₁ together with R forms a group -(CH₂)_q-, in which q is 2, 3, 4 or 5.

R₃ and R₄, which may be the same or different are independently hydrogen, C₁₋₆ linear or branched alkyl, C₁₋₆ alkenyl, aryl, C₁₋₆ alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, sulphonamido, C₁₋₆ alkoxyxcarbonyl, trifluoromethyl, acyloxy, phthalimido, amino, mono- and di-C₁₋₆ alkylamino, -O(CH₂)_r-NT₂, in which r is 2, 3, or 4 and T is hydrogen or C₁₋₆ alkyl or it forms with the adjacent nitrogen a group



in which V and V₁ are independently hydrogen or oxygen and u is 0, 1 or 2;
 -O(CH₂)_s-OW₂ in which s is 2, 3, or 4 and W is hydrogen or C₁₋₆ alkyl;
 hydroxyalkyl, aminoalkyl, mono- or di-alkylaminoalkyl, acylamino,
 alkylsulphonylamino, aminoacylamino, mono- or di-alkylaminoacylamino;
 with up to four R₃ substituents being present in the quinoline nucleus;
 or R₄ is a group -(CH₂)_t- when cyclized onto R₅ as aryl, in which t is 1, 2,
 or 3;

R₅ is branched or linear C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₄₋₇ cycloalkylalkyl,
 optionally substituted aryl, or an optionally substituted single or fused ring
 heterocyclic group, having aromatic character, containing from 5 to 12 ring
 atoms and comprising up to four hetero-atoms in the or each ring selected
 from S, O, N;

X is O, S, or N-C≡N.

2. A compound according to claim 1 in which:

Ar is phenyl, optionally substituted by C₁₋₆ alkyl or halogen; thienyl or a C₅₋₇
 cycloalkdienyl group;

3. A compound according to claim 1 in which:

R is C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylcarbonyl or hydroxy C₁₋₆
 alkyl.

4. A compound according to claim 1 in which:

R₁ and R₂ are each hydrogen or C₁₋₆ alkyl.

5. A compound according to claim 1 in which:

R₃ is hydrogen, hydroxy, halogen, C₁₋₆ alkoxy or C₁₋₆ alkyl.

6. A compound according to claim 1 in which:

R₄ is hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxy, amino, halogen,
 aminoalkoxy, mono- or di-alkylaminoalkoxy, mono- or di-alkylaminoalkyl,
 phthaloylalkoxy, mono- or di-alkylaminoacylamino or acylamino,

7. A compound according to claim 1 in which:
R₅ is phenyl, thienyl, furyl, pyrrol or thiazolyl.

8. A compound of formula (I) according to claim 1, or a salt or solvate thereof, in which:

Ar is phenyl, 2-chlorophenyl, 2-thienyl or cyclohexadienyl;

R is methyl, ethyl, n-propyl, -COOMe, or -COMe;

R₁ and R₂ are each hydrogen or methyl;

R₃ is hydrogen, methoxy, or hydroxy;

R₄ is hydrogen, methyl, ethyl, methoxy, hydroxy, amino, chlorine, bromine, dimethylaminoethoxy, 2-(1-phthaloyl)ethoxy,

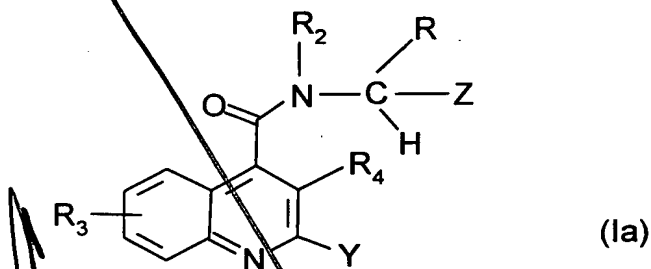
aminoethoxy, 2-(1-pyrrolidinyl)ethoxy, dimethylaminopropoxy,

dimethylaminoacetyl amino, acetyl amino, or dimethylaminomethyl;

R₅ is phenyl, 2-thienyl, 2-furyl, 2-pyrrol, 2-thiazolyl or 3-thienyl;

and X is oxygen.

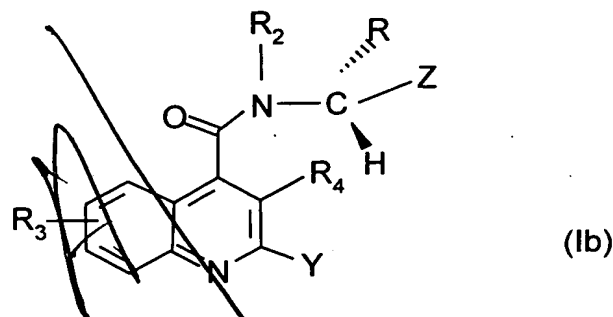
9. A compound according to claim 1, or a salt or solvate thereof, of formula (Ia)



in which

R, R₂, R₃ and R₄ are as defined for formula (I), in claim 1 and Y and Z, which may be the same or different, are each Ar as defined for formula (I) in claim 1.

10. A compound according to claim 9, of formula (Ib):



in which R, R₂, R₃ and R₄, Y and Z are as defined in claim 9.

5 9 14.

A compound according to claim 1 selected from the group consisting of:

- (R,S)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
- (+)-(S)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
- (-)-(R)-N-(α-methylbenzyl)-2-phenylquinoline-4-carboxamide;
- 10 (R,S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (+)-(S)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (-)-(R)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-
- 15 carboxamide;
- (R,S)-N-[α-(methoxycarbonyl)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α-(methoxycarbonyl)benzyl]-7-hydroxy-2-phenylquinoline-4-carboxamide;
- 20 (R,S)-N-[α-(carboxy)benzyl]-7-methoxy-2-phenylquinoline-4-carboxamide hydrochloride;
- (R,S)-N-[α-(methylaminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-thienyl)quinoline-4-
- 25 carboxamide;
- (R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(2-furyl)quinoline-4-carboxamide;
- (R,S)-N-[α-(methoxycarbonyl)benzyl]-2-(4-pyridyl)quinoline-4-carboxamide;
- 30 (R,S)-N-[α-(methoxycarbonyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α-(methoxycarbonylmethyl)benzyl]-2-phenylquinoline-4-

- carboxamide;
- (-)-(R)-N-[α -(methoxycarbonyl)-1,4-cyclohexadienylmethyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(1-hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide
- 5 single diast;
- (R,S)-N-(α -ethylbenzyl)-3-methoxy-2-phenylquinoline-4-carboxamide;
- (R,S)-N-(α -ethylbenzyl)-3-n-butyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]benzo-1,3-cycloheptadieno[1,2-b]quinoline-8-carboxamide;
- 10 (R,S)-N-(α -ethylbenzyl)-3-hexyl-2-phenylquinoline-4-carboxamide;
- (-)-(S)-N-(α -ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
- (+)-(R)-N-(α -ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-methoxyphenyl)quinoline-4-carboxamide;
- 15 (R,S)-N-(α -ethylbenzyl)-3-phenyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-fluorophenyl)quinoline-4-carboxamide;
- (R,S)-N-[α -(ethyl)-3,4-dichlorobenzyl]-2-phenylquinoline-4-carboxamide;
- 20 (R,S)-N-[α -(hydroxymethyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-(α -ethylbenzyl)-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-(α -ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide;
- 25 (R,S)-N-[α -(methoxycarbonyl)benzyl]-7-chloro-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]-6-methyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxymethyl)benzyl]-2-phenylquinoline-4-carboxamide;
- 30 (R,S)-N-[α -(methoxycarbonyl)benzyl]-6-chloro-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)benzyl]-3-ethyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-(α -n-propylbenzyl)-2-phenylquinoline-4-carboxamide;
- 35 (R,S)-N-(α -ethylbenzyl)-3-ethyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-(α -ethylbenzyl)-3-phthalimido-2-phenylquinoline-4-carboxamide;

- (R,S)-N-(α -ethylbenzyl)-3-n-propyl-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-6-bromo-3-methyl-2-(4-bromophenyl)quinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-6-bromo-3-methyl-2-phenylquinoline-4-carboxamide;
 5 (R,S)-N-[α -(methoxycarbonyl)benzyl]-6-methoxy-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-benzofuryl)quinoline-4-carboxamide;
 10 (R,S)-N-[(1,2-diphenyl)ethyl]-2-phenylquinoline-4-carboxamide;
 (R,S)-N-(α -trifluoromethylbenzyl)-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-3-methoxy-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-3-ethyl-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(ethyl)-4-chlorobenzyl]-2-phenylquinoline-4-carboxamide;
 15 (R,S)-N-[α -(methoxycarbonyl)benzyl]-N-methyl-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(3-thienyl)quinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-5,6-dihydrobenzo[a]acridine-7-carboxamide;
 20 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-pyrrolyl)quinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-thiazolyl)quinoline-4-carboxamide;
 25 (R,S)-N-(1-indanyl)-2-phenylquinoline-4-carboxamide;
 (R,S)-N-(α -n-butylbenzyl)-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(4-methylphenyl)quinoline-4-carboxamide;
 (R,S)-N-(α -heptylbenzyl)-2-phenylquinoline-4-carboxamide;
 30 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-methylphenyl)quinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(4-methoxyphenyl)quinoline-4-carboxamide;
 N-(1-phenylcyclopentyl)-2-phenylquinoline-4-carboxamide;
 35 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(4-hydroxyphenyl)quinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(3,4-

methylenedioxyphenyl)quinoline-4-carboxamide;
 N-(α,α -dimethylbenzyl)-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(ethyl)-4-methylbenzyl]-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(3-pyrryl)quinoline-4-
 5 carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(3,4-dichlorophenyl)quinoline-
 4-carboxamide;
 (-)-(R)-N-[α -(aminomethyl)benzyl]-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide;
 10 (-)-(S)-N-(α -ethylbenzyl)-3-chloro-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-3-bromo-2-phenylquinoline-4-carboxamide;
 (R,S)-N-(α -*iso*-propylbenzyl)-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-2-phenylquinoline-4-carboxamide;
 (+)-(R)-N-(α -ethylbenzyl)-2-phenylquinoline-4-carboxamide;
 15 (R,S)-N-[α -(methoxycarbonyl)benzyl]-6-fluoro-2-phenylquinoline-4-
 carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-cyclohexylquinoline-4-
 carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(3-chlorophenyl)quinoline-4-
 20 carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2-chlorophenyl)quinoline-4-
 carboxamide;
 (R,S)-N-(α -ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-8-acetyloxy-2-phenylquinoline-
 25 4-carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-8-hydroxy-2-phenylquinoline-4-
 carboxamide;
 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(2,4-dichlorophenyl)quinoline-
 4-carboxamide;
 30 (-)-(R)-N-[α -(methoxycarbonyl)-4-hydroxybenzyl]-2-phenylquinoline-4-
 carboxamide hydrochloride;
 N-diphenylmethyl-2-phenylquinoline-4-carboxamide;
 (-)-(S)-N-(α -ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide;
 (+)-(R)-N-(α -ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-
 35 carboxamide;
 (-)-(R)-N-[α -(methoxycarbonyl)benzyl]-3-hydroxy-2-phenylquinoline-4-
 carboxamide;

- (-)-(R)-N-[α -(dimethylaminomethyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(dimethylaminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- 5 (R,S)-N-[α -(aminocarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(1-pyrrolidinylcarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (-)-(R)-N-[α -(carboxy)benzyl]-2-phenylquinoline-4-carboxamide hydrochloride;
- 10 (R,S)-N-[α -(methoxycarbonyl)benzyl]-2-(4-chlorophenyl)quinoline-4-carboxamide;
- (R)-N-[α -(methoxycarbonyl)-4-methoxybenzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methoxycarbonyl)- α -(methyl)benzyl]-N-methyl-2-phenylquinoline-4-carboxamide hydrochloride;
- 15 (R,S)-N-[α -(methylcarbonyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(2-hydroxyethyl)benzyl]-2-phenylquinoline-4-carboxamide;
- (-)-(S)-N-(α -ethylbenzyl)-3-(2-dimethylaminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
- 20 (-)-(S)-N-(α -ethylbenzyl)-3-acetylamino-2-phenylquinoline-4-carboxamide;
- (-)-(S)-N-(α -ethylbenzyl)-3-(3-dimethylaminopropoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
- (-)-(S)-N-(α -ethylbenzyl)-3-[2-(1-phthaloyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride;
- 25 (-)-(S)-N-(α -ethylbenzyl)-3-(2-aminoethoxy)-2-phenylquinoline-4-carboxamide hydrochloride;
- (+)-(S)-N-(α -ethylbenzyl)-3-[2-(1-pyrrolidinyl)ethoxy]-2-phenylquinoline-4-carboxamide hydrochloride;
- 30 (-)-(S)-N-(α -ethylbenzyl)-3-(dimethylaminoacetylamino)-2-phenylquinoline-4-carboxamide;
- N-(α,α -dimethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide;
- N-(α,α -dimethylbenzyl)-3-amino-2-phenylquinoline-4-carboxamide;
- (-)-(S)-N-(α -ethylbenzyl)-5-methyl-2-phenylquinoline-4-carboxamide;
- 35 (R,S)-N-[α -(1-hydroxyethyl)benzyl]-3-methyl-2-phenylquinoline-4-carboxamide;
- (R,S)-N-[α -(methylcarbonyl)benzyl]-3-methyl-2-phenylquinoline-4-

carboxamide;

(R,S)-N-[α -(ethyl)-4-pyridylmethyl]-2-phenylquinoline-4-carboxamide;

(R,S)-N-[α -(ethyl)-2-thienylmethyl]-2-phenylquinoline-4-carboxamide;

(+)-(S)-N-(α -ethylbenzyl)-3-dimethylaminomethyl-2-phenylquinoline-

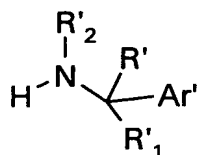
5 4-carboxamide hydrochloride;

(S)-N-(α -ethylbenzyl)-3-methyl-7-methoxy-2-phenylquinoline-4-carboxamide;

(S)-N-(α -ethylbenzyl)-3-amino-5-methyl-2-phenylquinoline-4-carboxamide;

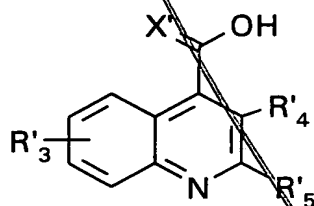
10 (S)-N-(α -ethylbenzyl)-3-methoxy-5-methyl-2-phenylquinoline-4-carboxamide.

12. A process for preparing a compound of formula (I) as defined in claim 1, or a solvate or salt thereof which comprises reacting a compound of formula (III)



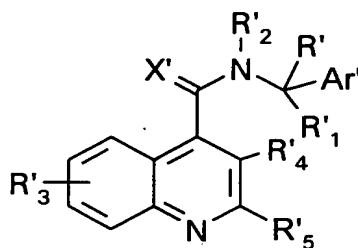
(III)

20 in which R', R'1, R'2 and Ar' are R, R1, R2 and Ar as defined for formula (I) or a group or atom convertible to R, R1, R2 and Ar, with a compound of formula (II)



(II)

25 or an active derivative thereof, in which R'3, R'4, R'5 and X' are R3, R4, R5 and X as defined for formula (I) or a group convertible to R3, R4, R5 and X, to form a compound of formula (Ic)



(Ic)

and optionally thereafter performing one or more of the following steps:

- (a) where R' , R'_1 to R'_5 , Ar' and X' are other than R , R_1 to R_5 , Ar and X , converting any one of R' , R'_1 to R'_5 , Ar' and X' to R , R_1 to R_5 , Ar and X to obtain a compound of formula (I),
- (b) where R' , R'_1 to R'_5 , Ar' and X' are R , R_1 to R_5 , Ar and X , converting any one of R , R_1 to R_5 , Ar and X to another R , R_1 to R_5 , Ar and X , to obtain a compound of formula (I),
- (c) forming a salt and/or solvate of the obtained compound of formula (Ic).

13. A process according to claim 12 in which the active derivative of the compound of formula (II) is an acid halide.

14. A pharmaceutical composition comprising a compound of formula (I) or salt or solvate thereof, as defined in claim 1, and a pharmaceutically acceptable carrier.

15. A method for the treatment and/or prophylaxis of pulmonary disorders (asthma, chronic obstructive pulmonary diseases -COPD-, airway hyperreactivity, cough), skin disorders and itch (for example, atopic dermatitis and cutaneous wheal and flare), neurogenic inflammation and CNS disorders (Parkinson's disease, movement disorders, anxiety and psychosis), convulsive disorders, epilepsy, renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression in mammals, which comprises administering to the mammal in need of such treatment and/or prophylaxis an effective amount of a compound of formula (I), or a solvate or salt thereof, as defined in claim 1.

16. A method for the treatment and/or prophylaxis of convulsive disorders, epilepsy, renal disorders, urinary incontinence, ocular inflammation, inflammatory pain, eating disorders (food intake inhibition), allergic rhinitis, neurodegenerative disorders (for example Alzheimer's disease), psoriasis, Huntington's disease, and depression in mammals, which comprises

administering to the mammal in need of such treatment and/or prophylaxis an effective amount of an NK₃ receptor antagonist.

Add
A3